



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/829,042

04/21/2004

Trevor Barrowcliffe

674583-2001

7419

20999 7590 06/15/2010
FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER

ROBINSON, HOPE A

ART UNIT

PAPER NUMBER

1652

MAIL DATE

DELIVERY MODE

06/15/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/829,042	Applicant(s) BARROWCLIFFE, TREVOR	
	Examiner HOPE A. ROBINSON	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 March 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4 and 6-8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4 and 6-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 April 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's response to the Office Action mailed September 2, 2009 on March 2, 2010 is acknowledged.

Claim Disposition

2. Claims 4 and 6-8 are pending and are under examination.

Claim Objection

3. Claims 4 and 6-8 are objected to because of the following informalities:

For clarity it is suggested that claim 4 is amended to read,

"A method of treating ~~[[h]]~~Haemophilia A or ~~[[h]]~~Haemophilia B, comprising administering by injection to a patient in need thereof ~~[[a pharmaceutically]]~~ an effective amount of a sterile pharmaceutical composition consisting essentially of coagulation ~~[[factors]]~~ Factors VIII and IXa, wherein the ~~[[presence of]]~~ coagulation ~~[[factor]]~~ Factor IXa ~~[[allows]]~~ reduces the concentration of coagulation ~~[[factor]]~~ Factor VIII in the composition ~~[[to be reduced]]~~ in comparison to a composition which does not comprise ~~[[a]]~~ coagulation ~~[[factor]]~~ Factor IXa, and wherein ~~[[the sterile pharmaceutical composition is administered to a]]~~ said patient ~~[[who]]~~ does not present with anti-coagulation ~~[[factor]]~~ Factor VIII antibodies".

For clarity it is suggested that claim 6 is amended to delete the phrase, "using recombinant DNA technology" and amended as followings, "The method ~~[[according to]]~~

Art Unit: 1652

of claim 4, wherein the coagulation ~~[[factor]]~~ Factor VIII ~~[[and IXa reagents are produced using recombinant DNA technology]]~~ is a von Willebrand Factor (vWF) B domain deleted rFVIII (recombinant Factor VIII).

For clarity it is suggested that claim 7 is amended as follows, “The method ~~[[according to]]~~ of claim 4, wherein the sterile pharmaceutical composition further comprises phospholipid”.

For clarity it is suggested that claim 8 is amended as follows, “The method ~~[[according to]]~~ of claim 4, wherein the sterile pharmaceutical composition is formulated to provide coagulation ~~[[factor]]~~ Factor VIII to ~~[[a subject]]~~ said patient at a dosage of between 2 and 10 IU/kg.

Correction is required.

Claim Rejections - 35 USC § 112

4. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The claimed invention is missing critical or essential information needed to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Claim 6 recites, “FVIII and FIXa reagents are produced using recombinant DNA technology”. The specification provides a similar discussion however, no specific methodology is provided as to how to produce the FVIII and FIXa which is needed to practice the method. The method is directed to treating haemophilia A or B by

Art Unit: 1652

administering to a patient a composition with FVIII and FIXa, thus how these two components are obtained is important in the method step.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. Claims 4 and 6-8 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claim 4 and the dependent claims hereto lack clear antecedent basis for the recitation of "... a patient who does not present with anti-coagulation Factor VIII antibodies" because the preamble of the claim requires administration to a patient in need thereof".

Claim 6 is indefinite for the recitation of "using recombinant DNA technology" because the claims are drawn to a method and thus the steps needed to perform the method should be outlined in the claim. It is unclear what technological steps are utilized to produce the required components of the method. Thus the metes and bounds of the claimed method is undefined. Claim 6 also lacks clear antecedent basis for the recitation of "the coagulation Factor VIII and IXa reagents" as this language is not provided in the independent claims.

Claim 8 lacks clear antecedent basis for the recitation of "a subject" because the independent claim recites "a patient in need thereof".

Maintained and Amended-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
6. Claims 4 and 6-8 remain rejected under 35 U.S.C. 103(a) as being obvious over Barrowcliffe et al. (cited on IDS) in view of Lang et al. (U.S. 5,506,112) taken with Capon et al. (U.S. 4,965,199).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art

Art Unit: 1652

only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

Barrowcliffe et al. found that FEIBA contained a form of Factor VIII that contributed 30% to 50% of the overall in vitro clot-promoting activity in inhibitor plasma. The results suggested that the Factor VIII may exist as a complex with Factor IXa and phospholipid and in this form may be partially protected from interaction with inhibitors. Barrowcliffe et al. also reported that the addition of purified Factor IXa and phospholipid could protect Factor VIII from subsequent inactivation by antibody and that the major protective effect was provided by the phospholipid (admitted prior art, see paragraph [0012] of the instant specification. Barrowcliffe et al. does not *per se* teach treating haemophilia, however, Lang et al. and Capon et al. provides such a teaching.

Art Unit: 1652

Lang et al. teach a method where a mixture of factor IXa, and phospholipids is added to a sample containing factor VIII (aqueous), thus activating Factor VIII to be assayed; and where subsequently activated factor VIII forms complex with factor IXa (see column 1, lines 8-14) and Capon et al. teach a method involving a step where Factor IXa initiates the conversion of Factor X to the activated form, Factor Xa; where Factor VIII is currently believed to function as a cofactor and is required to enhance the activity of Factor IXa. This step in the cascade is critical, since two most common hemophilia disorders have been determined to be caused by the decreased functioning of either Factor VIII (hemophilia A or classic hemophilia) or Factor IXa (hemophilia B). Therefore, Factor VIII is capable of catalyzing the conversion of Factor X to Xa in the presence of Factor IXa as well as correcting the coagulation defect in plasma derived from hemophilia A affected individuals (see column 10, lines 27-32). Lang et al. does not per se teach an injectable form. However, Capon et al. teach a composition that is free of contaminants, intended for a medicament to treat Hemophilia patients and provides a dosage that would fall within the recited range (paragraph 0188).

Therefore, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole, a method of treating hemophilia as recited in the claims because Barrowcliffe disclose the combination to FVIII and FIXa and the incentive to do so and Lang teach the same combination and the intention of using same as a medicament. Moreover, Capon, teaches FVIII and FIXa in combination and in a kit and dosage provided over an eight hour period that falls within the recited range. One of ordinary skill in the art would be motivated to combine the teachings of the reference

Art Unit: 1652

because each reference combines FVIII and FIXa and provide reasoning for said mixture being useful in the art. Moreover, the Supreme Court pointed out in *KSR*, “a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR*, 127 S. Ct. at 1741. The Court thus reasoned that the analysis under 35 U.S.C. 103 “need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the “inferences and creative steps that a person of ordinary skill in the art would employ.” *Id.* at 1741. The Court further advised that “[a] person of ordinary skill is...a person of ordinary creativity, not an automation.” *Id.* at 1742. Therefore, the claimed invention was obvious to make and use at the time the invention was made and was *prima facie* obvious.

Response to Arguments

7. Applicant's comments have been considered in full. Note that the rejections of record under 35 USC 103 remains, but has been amended to clarify the rejection. With regard to the rejection under 35 USC 103, Applicant state that the reference does not teach treating haemophilia. This argument is not persuasive as the collective teaching of the references renders the claimed invention as obvious. Note that the Lang et al. and Capon et al. references met this deficiency. In addition, Applicant state that the references do not teach a patient without anti-coagulation Factor VIII

Art Unit: 1652

antibodies. This argument is also not persuasive because Barrowcliffe et al. reported that the addition of purified Factor IXa and phospholipid could protect Factor VIII from subsequent inactivation by antibody and that the major protective effect was provided by the phospholipid. The 103 statute simply requires a mere teaching or suggestion and the combined teaching of the references renders the claimed invention as obvious. Moreover as set forth in KSR the court established that “a person of ordinary skill is...a person of ordinary creativity, not an automation”. Thus it would be obvious to treat patients that do not present with anti-coagulation Factor VIII antibody based on the teachings in Barrowcliffe et al.

Note that a new ground of rejection has been instituted as set forth above under 35 USC 112, first and second paragraph.

Conclusion

8. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811.

Art Unit: 1652

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Hope A. Robinson/

Primary Examiner, Art Unit 1652